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AMYOTROPHIC LATERAL SCLEROSIS.

By Joseph Collins, M.D.,
of New York.

Writing on amyotrophic lateral sclerosis in The American Journal of the Medical Sciences in June, 1896, I said: "The clinical picture which is called up by this name is a well-defined one, and not subject to remarkable variation. So much cannot be said for the pathological process upon which the disease is dependent, nor for the morbid anatomical conditions found at the termination of the disease." The truth of this statement is substantiated by the case which I herewith record. That it is no uncommon experience for the post-mortem investigation of a case to show that the disease clinically typical is not dependent upon the classical lesion, viz., degeneration of both motor neurons, constituting atrophy and disappearance of the anterior horn cells and degeneration of the pyramidal tracts, is abundantly verified by the reports of cases cited in my first paper.

Amyotrophic lateral sclerosis is a rare disease, among the rarest of all organic nervous diseases. In my clinic the diagnosis has been made only six times in five years, during which period about seven thousand new cases of nervous diseases have come under my observation. In view of the fact that recent investigations have shown that some cases reported clinically as typical examples of this disease have been found to be dependent upon syringomyelia, myelitis, and internal hydrocephalus, it is not unlikely that in some of these cases the diagnosis was erroneous. To show further the rarity of the disease in ten years at the City Hospital, where chronic nervous diseases are very common, I have not seen upward of six or seven cases. The disease has been known to physicians for more than a quarter of a century. Charcot and Joffroy first described it in 1869, but general knowledge of the disease dates from Charcot's classical description in 1874. Still very little is known of its natural history, and absolutely nothing of its etiology.

Before entering upon some discussion of the nature of the disease and its occurrence, I present the history of a case with clinical and anatomical details, which throws some light upon one or more of the questions concerning the evolution of this disease which are yet unsettled.

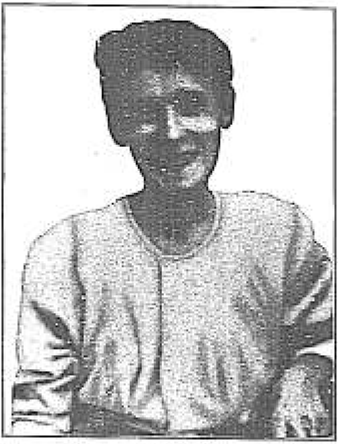
Clinical Summary. Woman, aged thirty-six years. First symptoms, pain in neck and head, weakness of the upper extremities and of the muscles that support the head; atrophy and fibrillary twitchings of the muscles of the shoulder girdle, neck, and hands; profound exaggeration of all the tendon jerks; muscular hypertonia; slight spasticity of the lower extremities, and slight contracture of the arms and hands; Babinski phenomenon; no trophic, sensory, or sphincter disturbances; early and profound bulbar manifestations; duration of the disease about three years.—The patient, a married woman, aged thirty-six years, accustomed to housework, came under my observation June 17, 1897. Her family history was not of interest save that her mother died of tuberculosis. No history of nervous disease could be elicited. She had never borne children; her sterility had been attributed to uterine disorder, for which she had received much treatment, five curettements, and one laparotomy. The major operation was in 1892, and one curettage a year since then. When she came to the clinic in June, 1897, she complained of severe frontal headache and pain in the back of the neck radiating to the top of the head; of a tired feeling of the neck and shoulders; of inability to bend the neck forward when sitting with the head leaning back against a rest, and to lift it from the pillow when lying, without the aid of the hands; of profound "nervousness," especially when excited or annoyed; of tremulousness and weakness of the hands, at times of the entire body, and of weariness. A journey like that to the clinic makes her very tired; light housework fatigues her, shopping makes her nervous, depressed, and prostrated; putting up the hair exhausts her.

She cannot fix the time exactly when these symptoms came on, for she has not been in good health for seven years. She is positive that the nervous symptoms have developed within the past two years. In this time she has lost weight steadily, thirty pounds altogether.

Examination at this time showed well-marked atrophy of the right supraspinatus muscle and slight atrophy of all the muscles of the right shoulder, and of the right hypothenar eminence. All of these muscles are the seat of fibrillary twitchings, and their mechanical irritability is much increased. Their response to electrical currents is very sluggish, especially that of the right supraspinatus. The change is a quantitative one, there being no real reaction of degeneration. Inability to use the right upper extremity is proportionate to the atrophy. It was noted that she carried the head peculiarly: in a fixed position, thrown slightly backward, the chin tilted upward. This, taken in connection with the difficulty she has in raising the head when lying, bespeaks involvement of the trapezii muscles. The grip of the right hand is weaker than the left. Both hands seem to have lost their dexterity. The knee-jerks are lively, the right more than the left, both pathologically increased. There is distinct ankle clonus on the right side, partial on the left side. The gait is not impaired, and she maintains that aside from weakness she walks as well as usual.

Sensibility unimpaired. The functions of the bowels and bladder are undisturbed. Deep pressure does not cause pain, although the atrophying muscles feel sore. The visual fields are normal, and there is no disorder of the special senses. The patient's voice is high-pitched, not modulated, and articulation is slightly impaired. Her features have a set expression, as if the emotional muscles were on the point of acting. (Fig. 1.)

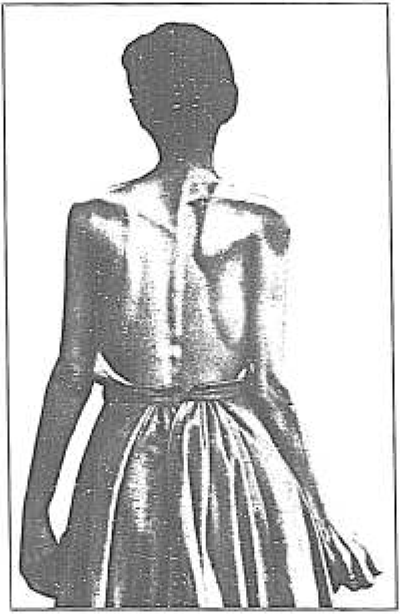
FIG. 1.



Illustrating the "spastic" condition of the emotional muscles.

In the autumn of the same year, six months after the above history was taken, it was noted that the patient complained of dyspnœa, dysarthria, palpitation, easily induced fatigue, dysmenorrhœa, profound nervousness, lack of will power, mental depression, suicidal impulses, increasing helplessness, and of difficulty in swallowing. If food gets on the back of the tongue it must be dislodged with the finger; if she gets it out into the anterior part of the mouth and then shoots the tongue back quickly the bolus goes down. This is exhausting. The face gets tired on chewing and talking. There is occasional regurgitation through the nose. The atrophy of the right shoulder girdle has increased, and extended so that now all of the muscles, including the trapezii, are involved. (Fig. 2.) The hypothenar eminence and other muscles of the hand are not more conspicuously atrophied than before. Fibrillary twitching of the muscles, not only of the atrophied muscles, but of others of the upper extremity that look normal, is very distressing. Myotatic irritability of all the muscles is very much increased, the knee-, ankle-, elbow-, and jaw-jerks being abrupt and exaggerated. The Babinski reflex is present. The gait is spastic, the stride slight, the strength feeble. The trunk is held rigid, the head fixed and tilted backward. The tongue is the seat of fibrillary tremor, and has the characteristic "bunched" appearance of atrophy. It can be protruded just beyond the lips. Intrabuccal motility is now much impaired. The lips have lost their alertness and can no longer be puckered. There is drooling at night. Vocalization and articulation are typical of bulbar paralysis. Attacks of dyspnœa, which are not infrequent, are most distressing to the bystander and agonizing to the patient.

FIG. 2.

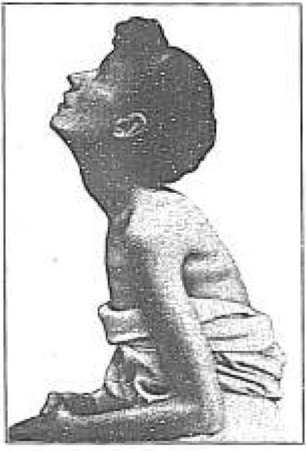


Showing extreme atrophy of shoulders.

The atrophy which the patient presented at this time is well shown by the accompanying photographs.

About this time she began to have profound hysterical attacks. The atrophy was now increasing rapidly. She had difficulty in maintaining the poise of the head. It tended when unsupported to fall backward or forward. (Fig. 3.) When the occiput approximated the nuchal region she could get the head forward by pushing it with the hands or giving a quick jerking motion forward, which set it up as if it were on a loose hinge. The atrophy of the muscles of the shoulder girdle on both sides was now so advanced that the heads of the humeri dropped from the sockets of the scapulæ, and there was proportionate limitation of movement.

FIG. 3.



Showing position of head when unsupported.

In the spring of 1899 she could still walk with short stride and slow step from one room to another with assistance. Spasticity of the lower extremities now first became considerable. During the entire course of the disease it was never prominent in the lower extremities, but now there was considerable resistance to passive movements, although the upper extremities had become quite powerless, but the bulbar symptoms predominated. The lips were decidedly atrophic. The tongue, which was before irregular and lumpy in its appearance, has become thin and ribbon-like, the seat of incessant vermicular movement. The soft palate, which cannot be raised voluntarily, is scarcely elevated on efforts of intonation, and swallowing is accomplished slowly and with great difficulty. Semisolids are taken most easily. They must be placed on the back of the tongue, then she swallows with great deliberation. Fluids are regurgitated through the nose sometimes, and attacks of coughing, incidental to some of the food getting into the trachea, are not uncommon. The tendon jerks were all enormously exaggerated, the slightest tap on the patellar tendon sufficed to throw the foot up sharply. The ankle-, elbow-, and jaw-jerks are likewise very much exaggerated. The Babinski reflex was distinctly to be obtained. There were still no sensory, sphincter, or trophic disturbances. Mentally the patient was very much as before, depressed, despairing, and dejected. Threats of suicide were constantly being made. Her reasoning powers were, however, undiminished.

Her emotional state had attracted attention from the beginning. She had no hope, except at rare intervals. Despite her despondency and threats of self-destruction, she was quite sound mentally. The attacks which she began to have about a year before death, and which I have called hysterical, were ushered in with palpitation, tachycardia, and dyspnœa, followed by screaming and violence, as if an expression of agony; stiffness, opisthotonos, unconsciousness, which graduated into sleep, out of which she awakened limp and exhausted. Such an attack would last several hours if not cut short by chloroform inhalation.

A description of one of these attacks, taken from the notes of her case, is as follows: "She becomes frightened, anxious, fearful, tremulous, complains of a feeling of suffocation and of great weight on the chest, and clamors for air. She moans, cries out, thrashes about, and gasps for breath, the respiratory acts being very rapid and labored. Some of the movements that she makes in these attacks are astonishing; for instance, she was lying flat, and with what seemed to be one supreme effort she raised her head and body and bent forward until her forehead struck the bed at her knees, and then she went back again, like the rebound of a ball, to the pillow. She had been unable to raise her head without the assistance of the hands for some time. The pulse in these attacks becomes so weak and feeble that it is scarcely countable. She is sleepless, restless, cast down, wants to die, but is continually clamoring to get well, and cannot be reassured.

The patient died May 25, 1899, after a paroxysm similar to that above described.

The autopsy was performed about four hours after death. Great difficulty was encountered in obtaining a post-mortem examination, and only the brain and spinal cord were examined. The autopsy notes are as follows:

The hair of the scalp is coarse and extremely sparse. The pupils are equal and dilated. The tongue is small, thin, and pale. The skin is smooth, and there were no abrasions. The weight of the entire body is forty-eight pounds. There is extreme atrophy of the muscles of the hands, forearms, and upper arms, and complete atrophy of the shoulder girdles. Some rigidity of the lower extremities. The muscles of the back and of the legs are very small but firm.

The brain was easily removed. It was of average size, and, aside from slightly increased consistency, it was normal macroscopically. The meninges were anæmic and apparently normal. The spinal cord to the naked eye presented a normal appearance aside from the increased consistency in the fourth cervical segment, to be described later.

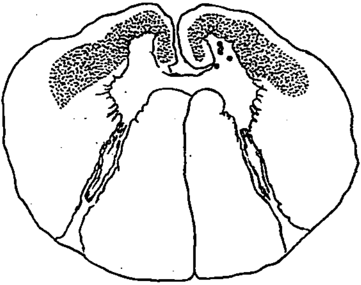
The cord was carefully segmented, and each segment divided into three pieces for alcohol, Marchi and Müller hardening. Thus preparations of Nissl, Marchi, Weigert, and picric acid fuchsin were obtained from each segment. Of the lower portion of the cord alternate segments were placed in various fixation fluids.

The oblongata was hardened in formaldehyde alcohol, and the brain in Lang's fluids. I am indebted to Dr. Carlin Philips, instructor of neurology in my clinic, for preparing the specimens—a very considerable task, painstakingly done.

In describing the histopathological changes I shall present briefly the picture of a few of the segments in series.

Second cervical segment, Weigert stain: The neuraxons constituting the columns are normal, with the exception of two symmetrical degenerated areas, as follows: A concentric zone encircling each anterior horn, beginning at the base of the anterior median fissure between the direct pyramidal tracts and the mesial border of the anterior horn, thence encircling the apex of the horn and extending nearly to the peripheral margin of the cord. (Fig. 4.) Thus the tracts involved in the degeneration are the antero-mesial and antero-lateral of the fundamental columns. Gowers' column, the direct pyramidal tract, and a thin marginal zone skirting the ventral periphery of the cord, are left intact. Although the degeneration spares the ventral marginal zone and the columns of Gowers, it is nevertheless possible that some neuraxons in both tracts may be involved. Scattered through the entire anterior and antero-lateral fundamental columns are many fibres which are normal in every respect. In sections stained with picric acid fuchsin one sees that the neuroglia proliferation is but slight in the areas that show such distinct degeneration with Weigert's stain. In one anterior cornua the motor cells, with the exception of two, have entirely disappeared, while on the other six are to be seen. The smaller cells of the lateral horn appear normal in number and structure.

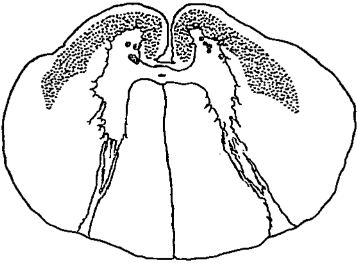
FIG. 4.



Second cervical segment, showing the extent of degeneration in the white substance.

In the third cervical segment the cornet-shaped area of degeneration is seen to extend dorsally to a greater extent in the lateral columns. (Fig. 5.) The absence of the motor cells is striking, the average number being about two in one anterior horn and four in the other. This great loss of anterior horn cells, from the upper portion of the second cervical to the lower portion of the third cervical, probably amounts to 90 per cent., and corresponds very well to the loss of function of the deep muscles of the neck. The small elongated cells of the intermediate zone appear to be normal in every way.

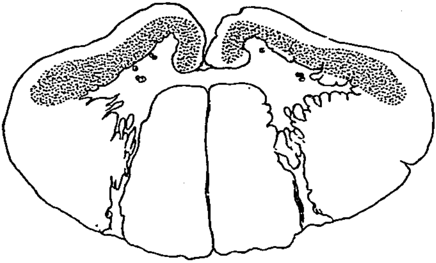
FIG. 5.



Outline drawing of the third cervical segment, showing extent of degeneration in the white substance.

In the fourth cervical segment the first striking change in contour and volume of the cord as a whole appears. (Fig. 6.) The deformity in outline is present in the following four or five segments below. It consists of an alteration of contour caused by a sinking in of the periphery at the point of emergence of the anterior roots. In fact, the periphery of the cord from a point corresponding to the apex of the anterior horn to the lateral tip assumes a concave instead of a convex line. Obviously the retraction of the ventro-lateral periphery of

FIG. 6.



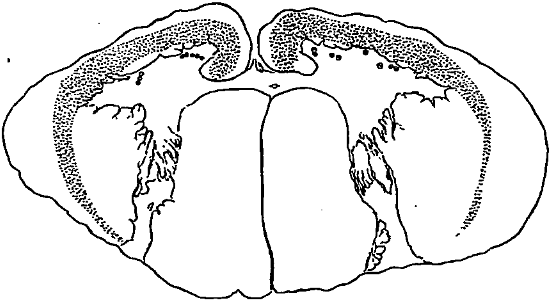
Fifth cervical segment, showing change in the contour and volume of the cord, scarcity of cells in the anterior horns (the cells are represented by circles), and degeneration in the white substance. (Composite drawing. Weigert stain for degeneration, carmine for the cells.)

the cord on either side of the anterior median fissure is due to the contraction of neuroglia growing in the degenerated area described. Inasmuch as this deformity of the cord's contour is not present in the second and third cervical segments, we may assume that the neuroglia in these t) segments is of more recent origin than that in the fourth segment.

The area of the degeneration shows some further variation from the previous segments on account of change of shape of the ventral horns of gray matter, the gray matter of the fourth cervical segments extending laterally so as to thrust the lateral horn toward the periphery. The degenerated area from here on thus assumes a sickle shape. (Fig. 7.)

Another respect in which this segment differs from those above is in the degeneration of the marginal zone just ventral to the mesial and lateral boundary of the anterior horn. Aside from these degenerative changes in certain areas as described, the remainder of the white substance appears to be normal.

FIG. 7.

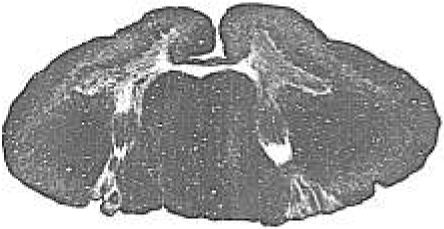


Sixth cervical segment, showing sickle-shaped area of degeneration.

Sections from this level stained by the Nissl method show only three or four large motor cells in each ventral horn. This is an extraordinary decrease in the number of cells, as in the normal cord one can count fifteen to twenty-five. The number of medium-sized and small cells in the region of the gray commissure is not so greatly reduced. In contrast to the findings in other levels of the cord, the lateral horn group at this level is entirely absent. As regards the histological process which caused the disappearance of these cells, the serial phases of it are difficult to formulate, for the reason that the cells that are present are fairly normal. While it is obvious that thousands of cells have disappeared, it is nevertheless difficult to find a single cell body which is actually going to pieces or which shows unmistakable evidences of disintegration. The question is, "How do they disappear?" We find no particular evidence of their destruction, and yet with even a low-power inspection the most striking feature of the whole case is the absence of these cells without a trace of their existence. The remaining cells usually show some confluence of chromophilic plaques into a homogeneous mass and yellowish pigment granules which are crowded off into one pole or extremity of the cell. But between this condition of the cell and its ultimate disappearance no intermediate phases can be found.

A brief summary of the findings in Nissl preparations may be made as follows:

FIG. 9.



Weigert stain of the eighth cervical segment, showing deformity of the anterior horns.

1. A fair proportion of the anterior horn cells that have escaped destruction show no great departure from the normal except fogginess and indistinctness of outline of the chromatic plaques.
2. Other cells show confluence of plaques and have masses of yellowish pigment in the protoplasm. The cells of this second class apparently are atrophic. These are illustrated in Fig. 8.

FIG. 10.

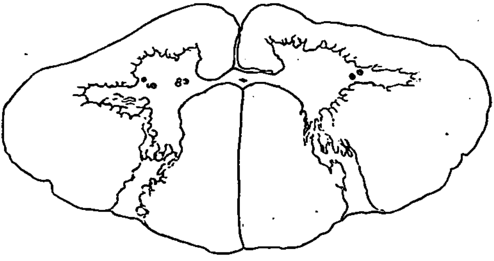
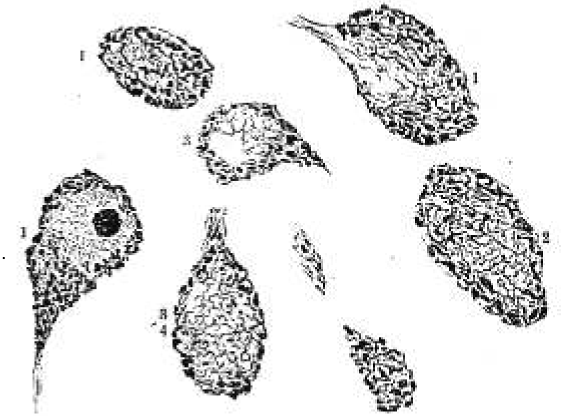


Diagram of the seventh cervical segment, to show paucity of cells in the anterior horns.

Fifth cervical segment practically the same as the fourth cervical.

Sixth cervical segment. In this segment the degeneration extends dorsally in a symmetrical way, forming a tongue-shaped area between the crossed pyramidal and the direct cerebellar tracts, reaching to the end of the posterior horn. The anterior horns are more flattened than in their normal condition, and lie nearer to the ventral periphery

FIG. 8.

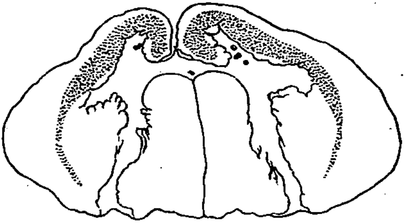


Cells of the anterior horns, showing indistinctness of outline (1, 1, 1) of chromatic plaques; masses of yellow pigment (2): plasmolysis (3, 3); chromatolysis (4).

of the cord. The large motor cells of this segment as seen in Nissl preparations show some diminution in number, corresponding proportionately to those observed in the preceding segment; also, the lateral horn group of cells has disappeared.

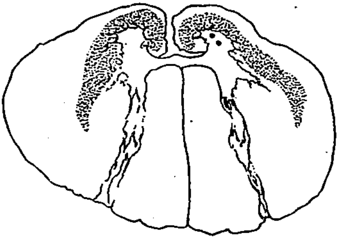
In the seventh and eighth cervical segments the area of degeneration of white fibres has the same relative distribution, except that it reaches further inward toward the lateral horn. The anterior roots show marked degeneration when examined by Weigert's method. (Fig. 9.) The cells of the anterior horn are very few (Fig. 10), and are degenerated as well as the groups of cells in the lateral horns. (Fig. 11.) The direct cerebellar tract in this segment shows a few degenerated fibres.

FIG. 11.



To show the area of degeneration in the white matter at the eighth cervical segment.

FIG. 12.

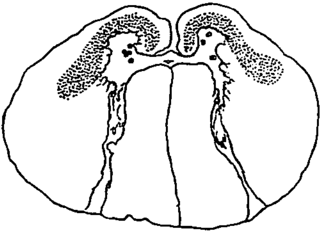


First dorsal segment, to show the progressive diminution of the area of degeneration in the white matter.

From the level of the first dorsal to the fourth, inclusive, the type of fibre degeneration takes the form shown in the upper cervical region, namely, a zone encircling the anterior horns, becoming progressively smaller and less and less intense, until at the level of the fourth dorsal it is scarcely discernible, except for a slight and ill-defined pallor encircling the apex of the ventral horns. (Figs. 12, 13, and 14.)

The disappearance of the motor cells is somewhat more difficult to determine throughout these first four dorsal segments than in the cervical segments, since normally there are so few cells in the ventral horns. There can be little doubt, however, that the atrophy of the cells is present in these segments in about the same proportion as in the cervical cord. The lateral horn cells and those of Clarke's column appear to be normal in these segments.

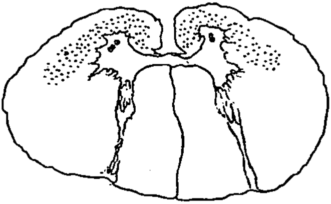
FIG. 13.



Second dorsal segment, to show the progressive diminution of the area of degeneration in the white matter.

From the fifth to the eleventh dorsal segments the degeneration of the fundamental columns is so slight that it is hardly apparent in sections stained by Weigert's method, yet in picric acid fuchsin specimens there is seen to be present an increase in neuroglia tissue. This confirms the idea that the same degeneration exists, but to a less extent, throughout the entire dorsal region.

FIG. 14.

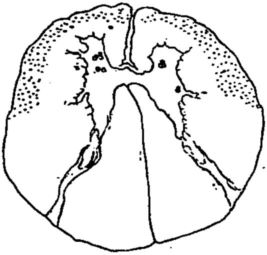


Third dorsal segment. Stippled area corresponds to the degeneration.

What has been said regarding the condition of the motor cells of the upper dorsal also applies to segments of the lower dorsal region. The cells of the lateral horn are normal, while here and there in Clarke's column are groups of cells which are atrophic and are pigmented, with excentric nuclei.

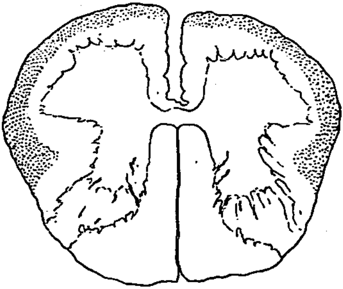
From the twelfth dorsal to the third sacral, inclusive, the zone of degeneration in the ventral half of the spinal cord assumes a radically different position from that found in other regions. (Fig. 15.) It occupies the peripheral lamina of the ventral half of the cord extending from the lips of the anterior fissure around to a point opposite the apex of the lateral horn, where it expands to a triangular mass indenting deeply inward the region of the cord just ventral to the crossed pyramidal tracts. It may be briefly described as a comma-shaped area, the head of the comma lying against the ventro-lateral border of the crossed pyramidal tracts, and the attenuated tail of the comma extending thence around the periphery of the cord nearly to the lips of the anterior median fissure. (Fig. 16.)

FIG. 15.



To show the degenerated area approaching the periphery.

FIG. 16.



Showing the area of degeneration in the lumbar cord.

Relatively speaking, the anterior horn cells throughout the lumbar and sacral regions of the cord are as much diminished in number as in the cervical region. Because the lower extremities were active long after the involvement of the upper ones, we had expected that the lumbar and sacral regions of the cord would show a corresponding immunity from disease of the anterior horn cells, but such is not the case. I was again disappointed in not finding stages of cell atrophy which would enable me to determine the actual process of dissolution of the cells. Here, as elsewhere in the cord, the cell is either fairly normal in appearance or it has completely disappeared. Throughout the cord the bloodvessels seen are normal.

In the medulla oblongata, from the sections taken at the lower one-fourth of the hypoglossal nucleus, one cannot say that there is any striking loss of the cells. Certainly there is no such loss in this nucleus to correspond with the striking loss of motor cells of the cord. There are, however, positive signs of structural changes, although these are limited to a small proportion of all the cells. Those affected show eccentricity of the nuclei, homogeneous conversion of the chromophilic plaques, or a filling up with pigment granules. I am unable to record any signs of cell disintegration, such as shrinkage or distortion of the cell body. These same anatomical findings are present in the nucleus ambiguus. From the scattered and isolated distribution of this nucleus it is quite impossible to say that degeneration of it exists in a given instance unless it is practically destroyed. Such is not the condition in this case.

The dorsal vagus nucleus is apparently normal. In Weigert preparation of the oblongata from this region the posterior longitudinal bundle is seen to be slightly but distinctly degenerated. This is what we might expect from its relation to the anterior and lateral ground bundle of the cord. Aside from these changes the oblongata was normal. The internal capsule and the corpus callosum were not examined.

Pieces of the motor cortex hardened in Lang's fluids were examined. The large motor cells from the paracentral lobule and from the Rolandic area show a pallor which at first seems to be indicative of structural change. It appears that this change is not confined to these cells, but affects uniformly all the cells of the cortex. These cells are quite as numerous as normal, so having used such an unsatisfactory reagent as Lang's mercuric hardening fluid we concluded that the change is an artefact rather than a true structural change. No statement can, therefore, be made as to the presence or absence of pathological changes in the brain.

The pathological findings of this case may be summarized as follows:

1. Uniform disappearance of the ventral horn cells throughout the entire cord, affecting (possibly) the dorsal region less severely than the cord enlargements.

2. Degeneration of a zone in the anterior fundamental columns skirting and encircling the ventral horns in the cervical and upper dorsal regions, also the anterior portion of the lateral limiting layers. (Bechterew.)

3. Degeneration of a marginal strip of the ventral periphery of the cord expanding dorsally against the ventral and lateral border of the crossed pyramidal tract, and appearing with a comma-shaped head in the lumbar and sacral regions.

4. Deformity of the ventral face of the cord in the cervical and upper dorsal region due to a concave sinking-in of the periphery.

5. Neuroglia proliferation in the degenerative area of white matter, and also in the anterior horns of the cord enlargements.

6. Evidence that the neuroglia proliferation is older in the cervical region. The degeneration is denser in the region and has caused shrinkage of the ventral face of the cord at the emergence of the roots.

7. Atrophy of the anterior roots.
8. Distinct evidence of cell degeneration (chromatolysis, plasmolysis, and disintegration) in the hypoglossal nucleus and the nucleus ambiguus.
9. The pyramidal tracts are intact.

Amyotrophic lateral sclerosis is a disease characterized by the symptoms of progressive muscular atrophy of the Aran-Duchenne type, complicated with bulbar involvement, plus spastic paresis, particularly of the lower extremities, and exaggeration of the tendon jerks all over the body. The morbid process upon which it is dependent consists in a decay of the peripheral motor neurons in the ventral horns, the terminal arborizations of the central motor neuron (in other words, the ending of the neuraxons that come down through the cord as pyramidal tracts), and of the pyramidal tracts themselves, and atrophy of the column (strange cordonal) and commissural cells of the gray matter. The degeneration extends centrifugally in the peripheral motor neurons, centrifugally and centripetally in the central motor neurons. This constitutes when the process is complete a characteristic microscopic picture, the principal features of which are (1) atrophy of the anterior horns and diminution or disappearance of all its cell constituents without noteworthy change in the bloodvessels; (2) degeneration of the fundamental tracts of greater or lesser extent; and (3) degeneration of the pyramidal tracts which may be so slight as to be scarcely detectable, or so complete that it may be traced to the origin of these tracts in the motor cortex. The question whether the peripheral motor neuron—*i. e.*, the root cells of the anterior horns, or the central motor neurons—the pyramidal tracts—are the first to be involved, cannot yet be answered.

Neurologists are well aware that there is much difference of opinion as to the starting-point of the disease. Charcot and the Parisian school generally, with the exception of Brissaud, maintain that the lesion is primarily and predominantly (at least in the beginning) of the central motor neurons, the pyramidal tracts in the spinal cord being diseased first, and that the affection of the white matter is consecutive or "deuteropathic." Brissaud's idea seems to be that the primary seat of the disease is in what Marie calls the supplementary zone, an area ventral to the pyramidal tracts and dorsal to the intermedullary anterior roots made up of the prolongations of column cells in the gray matter uniting different levels of the cord. The pyramidal fibres are involved later, and, finally, the ventral horn cells. This, however, presupposes the secondary involvement of the gray matter, which is the question in point. Dejerine and Thomas, commenting upon this view, say that this opinion of Brissaud is invalidated by the facts. The fact that the lesion of the motor cord is not strictly confined to the pyramidal tracts, but invades the antero-lateral, speaks in favor of Charcot's view. They then proceed to say that the degeneration of the pyramidal tract in amyotrophic lateral sclerosis is for them indisputable, because they have always found it. This is a denial of the validity of the work of others as well as an expression of finality that few scientific men permit themselves.

Leyden was the first to contest this teaching of Charcot, and he has unswervingly maintained his position. His view is that the peripheral motor neuron is first and predominantly affected, and that the changes in the white matter are sequential. This view is shared, in a measure at least, by many of his countrymen. Gowers teaches practically a similar doctrine, namely, that amyotrophic lateral sclerosis is a variety of progressive muscular atrophy in which the pyramidal tracts are more profoundly affected than they are in the ordinary form of spinal progressive muscular atrophy. This is the view held by many neurologists in this country, for instance, Dana and Sachs.

As a matter of fact, it is impossible to say dogmatically, from histological study of our cases, whether the peripheral or the central neuron is affected first. The truth is probably that in one case the central neuron is diseased first, and in the other the peripheral. When the central neuron is affected first it is likely that the degenerative process begins in the central convolutions and not in the cord. This involvement of the cell body of the central motor neurons causes decay of the entire neuron, beginning in the most remote part—that is, in the spinal cord, the pyramidal tracts, the intercalary neurons, and the terminal ramifications around the anterior horn cells. The fact that the degeneration of the pyramidal tracts progresses upward does not speak against the primary cortical involvement; in fact, it speaks rather in favor of it.

It seems to me that we must admit, because of such a case as the one published herewith, that the lesion in some cases of amyotrophic lateral sclerosis begins in the cells of the anterior horn, and that destruction of the cells therein situated causes the phenomena (in part at least) of the disease, and accounts for the pathological findings. The cells of the anterior horns are of three distinct varieties. First, those which give rise to the anterior roots of the spinal nerve (root cells); second, those that send their prolongations from one side of the cord to the other (commissural cells); and, three, column (cordonal) cells—cells whose prolongations bind one segment of the cord to another by means of so-called association fibres. It is the degeneration of these column cells that causes the area of degeneration in the white matter of the cord in our case. Decay of other fibres, such, for instance, as the fibres of the column of Gowers, was probably incidental to the destruction of these short fibres. It is well known that column cells are to be distinguished from root cells not only by their histological peculiarities, but by their location. They are particularly numerous in the enlargements of the cord, and they occupy a region in the middle of the anterior horn close to its junction with the posterior horn ventral to the column of Clarke, and to the column of cells described by Onuf and myself in the cat, which we called the paracentral column. The adjacency of these cells to the column of Clarke accounts for the existence of changes in the direct cerebellar tract in some cases which have been described, the lesion of the column cells implicating by contiguity some of the cells of Clarke's columns.

Destruction of these cordonal or column cells causes the degeneration of the fundamental columns in cases of amyotrophic lateral sclerosis and progressive muscular atrophy of the Aran-Duchenne type. That such degeneration does not occur in every case of either one of these diseases in no way invalidates what has been said. In the majority of cases of spinal progressive muscular atrophy such degeneration does not occur, and the explanation is that in such cases the destructive lesion in the spinal cord confines itself to the root cell (*i. e.*, to the ventral portion of the anterior horns), and that the column cells are not implicated. When they become implicated the supplementary zone in the gray matter is found diseased, as was the case in some observations of J. B. Charcot. It is not unlikely that this explanation suffices for all the cases of progressive muscular atrophy with changes in the white matter.

As to the explanation of the spasticity and exaggerated reflexes in a case like ours or that of Wolff, it must be sought for in some alteration to the central motor neuron in the brain which has not as yet extended to such a degree as to cause discernible alteration of its prolongation in the spinal cord.

What has been said should not be construed to mean that the lesion of amyotrophic lateral sclerosis is not often, perhaps always, if the disease lasts long enough, a degeneration of both systems of neurons throughout their entire course. That this is so there cannot be the shadow of a doubt. There are now eleven cases on record (the two cases of Kojewnoff, two of Charcot and Marie, one each of Lennmalm, Lumbroso, Nonne, Strümpell, Mott, Hoche, Spiller, Czyhlarz and Marburg) in which the pathological process involved both systems of neurons in their entirety. My contention is merely that such involvement is not necessary for the existence of the disease clinically. It may exist in its most typical form without any involvement of the pyramidal tracts whatsoever. This is shown by the cases of Wolff and Senator and by my own case. The case reported by Senator and by Wolff was clinically a fairly typical case of amyotrophic lateral sclerosis, especially in the latter stages. On microscopic examination of the specimens there were found atrophy of the anterior horn cells, arterial and venous hyperæmia, multiple punctate hemorrhages, apparently of recent origin, and incipient syringomyelia in the lumbar cord. The changes in the motor spinal cells explain the atrophy in this case, but there is no adequate explanation of the spasticity. Dercum and Spiller, in commenting upon this case, inquire if they may not venture to suggest that the foci of softening around the hemorrhages had something to do with causing the spasticity. But Wolff has already considered this. In the first place, the softening was almost exclusively of the gray substance around the junction of the anterior and posterior horns, and of the posterior roots. That it could not have been due to the hemorrhages is shown by their recent occurrence. To explain the spasticity it may be fair to assume some involvement of the central motor neurons in the cortex which has not yet gone on to decay sufficient to produce degeneration at their termini. That spasticity may be caused by cerebral lesion without degeneration of the pyramidal tracts is well known. It occurs sometimes with hydrocephalus and with brain tumor, such as in a case diagnosticated as lateral sclerosis, recorded by Schultz, in which the autopsy showed only internal hydrocephalus. There was no trace of spinal-cord degeneration.

When the disease process of amyotrophic lateral sclerosis has reached its completion there can be no doubt, I think, that both motor neurons and the nerve elements which unite the motor nuclei of different levels together are involved, and this constitutes the typical lesion of the disease. Our case may be looked upon as one which stands midway between the cases in which the pyramidal tracts are pronouncedly affected and the case reported by Wolff. For a long time it was doubted that primary sclerosis existed as a pathological entity, although it had long been recognized clinically. The cases of Minkowski (*Deutsches Archiv f. klinische Medicin*, vol. xxxiv. p. 24) and of Dejerine and Sottas came near to fulfilling the requirements, but it was not until Strümpell, Donaggio (*Rivista Sperimentale di Freniatria*, 1897, vol. xxxiii.), and Kuhn (*Deutsche Zeitschrift f. Nervenheilkunde*, vol. xxxii. p. 144) published their cases that there was full substantiation of the existence of this condition. Primary lateral sclerosis must be a very rare disease, but not many years since the diagnosis of lateral sclerosis was not an uncommon one. Now it is rarely made. Careful following up of the cases in which such diagnosis was made has shown that they prove to be examples either of amyotrophic lateral sclerosis or multiple sclerosis; more the former than the latter. Moreover, since the establishment by Erb of the disease known as syphilitic spinal paralysis, some of the cases formerly diagnosticated as lateral sclerosis have found their proper classification there.

The changes in the spinal cord in amyotrophic lateral sclerosis are by no means confined to the anterior horns and the pyramidal tracts. The posterior columns, especially the columns of Goll, have been found diseased a number of times. For instance, the cases reported by Oppenheim, Charcot and Marie, Hektoen, Brissaud, Dercum and Spiller, Luce, Dejerine, and Sottas. What the significance of these degenerations in the posterior columns is it is not possible to say. It may be that tabes has been superimposed upon amyotrophic lateral sclerosis, or *vice versa*, such as in a case of progressive muscular atrophy plus tabes about to be reported by me. It may be that the neuroglia overgrowth in the cord chokes off some of the fibres making up the columns of Goll, or it may be, as Marie suggests, that the cells of the gray matter that send their axis-cylinders into the posterior columns may be diseased, and thus cause decay of their prolongations.

The direct cerebellar tracts have occasionally also been found implicated by the morbid process. Stadelman was one of the first to call attention to the fact that degeneration of the lateral columns extends in some instances far beyond the confines of the pyramidal tracts, and this has been corroborated by many other observers, particularly by Marie, by Raymond and Ricklin, Spiller, Schlesinger, and others. Oppenheim gave what is probably the correct interpretation of this degeneration of the supplementary zone—*i. e.*, that it is due mainly to atrophy of short fibres uniting segments of the cord to one another.

That amyotrophic lateral sclerosis is a different disease from progressive muscular atrophy of the Aran-Duchenne type must be admitted, I think, also because of its very different clinical delineation. It is difficult to conceive of two diseases whose clinical course is more unlike. Progressive muscular atrophy of the Aran-Duchenne type is slow in its course, oftentimes lasting from five to fifteen years. Amyotrophic lateral sclerosis rarely lasts more than from two to three years. Of course, there are cases, such as that of Dejerine and Thomas, which last much longer, but these are exceptional. A patient with muscular atrophy does not seem to be ill for a long time after the onset of the disease, while in amyotrophic lateral sclerosis he is ill from the very beginning. In the latter there are no periods of cessation of progress or remission, such as there is not infrequently in spinal progressive muscular atrophy. And, finally, the different specific clinical features which differentiate the two conditions need not be here enumerated, as they are too well known. But that the two conditions cannot always be differentiated is well shown by an experience of Raymond. The twelfth lecture in the fourth series of his *Clinique des Maladies du Systeme Nerveux* is devoted to a case of progressive muscular atrophy of the Aran-Duchenne type. Under diagnosis the author says: "Il s'agit indubitablement d'un cas d'atrophie musculaire progressive." The autopsy showed (report published with the series of cases reported to the last International Congress in Paris, 1900, by Phillipe and Guillain) that the lesion was that typical of amyotrophic lateral sclerosis. When the case was examined by Raymond the exaggeration of the reflexes which had previously existed had disappeared.

There are cases of amyotrophic lateral sclerosis in which the spastic symptoms precede the atrophic manifestations, and others in which they predominate. Such cases bespeak an earlier or more profound involvement of the lateral columns than of the gray matter. Moreover, there are trustworthy records of many cases in which the degeneration of the pyramidal tracts was complete, while the process of the disease in the gray matter was still in a state of progression.

It is not easy to understand why there should be so much and such acrimonious discussion as to whether the gray matter or the white is first to be involved. In amyotrophic lateral sclerosis we are dealing with a poison or noxious influence which is capable of causing destruction of two distinct portions of the spinal cord which are rarely diseased simultaneously—the white and the gray matter. If this is admitted, why should not one of them be diseased first in one instance and the other in a second instance?

Whether amyotrophic lateral sclerosis is a part of or a variety of spinal progressive muscular atrophy is another question, and a question which, as I have indicated above, must, it seems to me, be answered in the negative. Although spinal progressive muscular atrophy may be accompanied by disease of the white fibres of the cord which on microscopic examination reveals itself as a degeneration of the supplementary zone, there is never any such degeneration of the pyramidal tracts as that ordinarily found in cases of amyotrophic lateral sclerosis. I do not recall that any case has been recorded in which degeneration ot the central motor neuron throughout its entire extent existed. So that from a clinical as well as from an anatomical standpoint it seems the identity of these two diseases must be denied. A little later on we shall see that a consideration of the etiology leads to the same conclusion.

The clinical picture of amyotrophic lateral sclerosis is a very constant one, and liable to but slight variation. The symptoms are typified by the case reported in detail in this paper, so that they do not call for repetition here. In looking through the literature of the subject I have been impressed with the frequency with which mental symptoms have been observed. By this I do not mean cases in which the disease has developed in insane persons, such as in the case of Sarbo and of Dornbluth. Amyotrophic lateral sclerosis may develop in an insane person as well as in a person of sound mind. I am inclined to think that it is an error to classify such cases as that reported by Zacher as a typical form of the disease. A man of thirty developed six years after syphilitic infection disturbance of speech, and later the clinical picture of general paresis, which was accompanied with atrophy in the upper extremity. The autopsy, in addition to many other lesions, revealed changes in the crossed pyramidal tracts and slight alteration of the anterior horns. Nor do I think that such cases as the one recently reported by Jurman as one of amyotrophic lateral sclerosis supervening in a general paretic after a blow on the jaw which caused a fracture should be included with this disease at all. Jurman's patient developed difficulty of swallowing and of speech, inability to put out the tongue, feebleness of the arms and legs, augmentation of the tendon-jerks, clonus of both feet, difficulty in walking, slight diminution of faradic irritability, and forced laughter. I can see nothing in a symptom-complex such as this incompatible with general paresis. Bearing in mind the widespread and extensive decay of neurons which characterizes general paresis, it is far more legitimate to classify such cases under that disease than to try to put them under the rubric of amyotrophic lateral sclerosis.

The mental symptoms of amyotrophic lateral sclerosis that are worthy of mention are suicidal impulse, such as existed in my case, attacks of meaningless laughter and of weeping without direct cause, occurring in an impulsive manner, and evidences of slight dementia. All of these symptoms may well have their foundation in the organic changes that go on in the brain. It is not improbable that the impulsive, uncontrollable emotional display bespeaks an involvement of the motor neurons extending into the thalamus. In a similar way such cerebral manifestations as those reported in a case by Erben, paraphasia and disturbance of speech and intelligence, may be attributed to disease of the corticomuscular neurons. The point that may be emphasized here is that mental symptoms occur with considerable frequency in this disease and rarely in spinal progressive muscular atrophy.

THE ETIOLOGY OF AMYOTROPHIC LATERAL SCLEROSIS. The etiology of amyotrophic lateral sclerosis is very obscure, practically nothing is known of the real cause of the disease, and I regret that I am unable to contribute anything. Whatever information is to be derived from a study of a considerable number of cases will, however, be here set forth. After careful examination of the entire literature of amyotrophic lateral sclerosis, I have selected the records of ninety-four typical cases and added to them ten of my own cases, five with autopsy and five without, and have made these the basis of a statistical study.[1]

Of the 104 cases 55 were males and 49 females. It will be seen at once that this is at variance with the statements of many previous writers regarding its frequency in the two sexes. The French school particularly are positive in their statement that the disease is much more frequent in females than in males. Probst, who made a careful analysis of 53 cases in 1898, found that the number was evenly distributed between males and females. As my cases are in nowise selected, merely taken from the literature wherever a typical case could be found, the inference is more reliable than from a small number of cases personally observed. For instance, of the last 7 cases that I have seen personally 5 were men and 2 women.

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[1] Dr. Joseph Frankel has kindly loaned me the histories of three typical cases, which are incorporated.

It is generally held (and I have heretofore shared the view) that amyotrophic lateral sclerosis is more frequent between the ages of thirty and forty. In 100 unselected cases 30 patients were between thirty and forty; 29 between forty-five and fifty; 28 between fifty and sixty, and 2 under thirty. This would seem to show that the decade following the forty-fifth year is equally liable to the affliction.

In 26 cases the total duration of the disease was fifty-five years, which makes the average duration a little more than two years. This coincides with my experience. The briefest duration of the disease in cases found in the literature was five months, and this patient was carried off by influenza. In 2 cases, however, the disease seems to have run its course in six months. Record of 4 cases was found in which the disease lasted only nine months. A few cases only lasted upward of five years; the longest on record seems to be ten years.

The part of the body to be first affected was inquired into with considerable interest. Out of 81 cases in which there was specific information on this point the upper extremity was affected first in 39 cases, the lower extremity in 14 cases, and the upper and lower extremity (hemiplegic), or all four extremities, in 11 cases, while the disease came on with bulbar symptoms in 21 cases. In upward of 50 per cent. of all the cases bulbar symptoms appeared within the first year. But in the cases that are ushered in with bulbar symptoms it is not long before atrophy or spasticity or both show themselves in other parts of the body.

Patients are very apt to attribute their symptoms or disease to influence or experience known to be deleterious to their health, such as exposure to the wet or cold. This is the case particularly when the seemingly attributable cause precedes immediately the appearance of the first symptoms. Exposure to cold and wet, overwork, strife, fright, and bodily injuries were enumerated as causative in 28 instances. In many of the cases on our list no attributable cause is given. Bodily injury was said to have preceded the first manifestations of the disease in seven instances; but the relationship of injury is often very remote, as in the following case:

J. E., aged forty-five years, shoemaker, married, born in Russia; dates the beginning of his illness to July, 1897. He attributes it to a fall from a car three months before, which, however, produced no apparent injury. He complains of weakness in the hands and feet and of difficulty in speech. He has had considerable vertigo, headache, and nervousness, and lately difficulty in swallowing and chewing has been noticed. He complains also of a "drawing" sensation in the legs and hands, of a sensation of coldness in the lower half of the abdomen, and of heat in the upper half of the body, which is also the seat of profound perspiration. In September, 1897, an examination showed typical spastic gait, short, wooden stride, locomotion being accomplished with great difficulty. Fibrillary twitchings of the shoulder girdles are very conspicuous. The patient is unable to close the mouth tightly on account of fibrillary twitching of the face and weakness of the lip muscles. There is no atrophy.

On March 2, 1898, an examination was made, of which the following is a transcript of the notes:

The patient is of medium size, fairly well nourished, except in the localities where muscular atrophy has reduced the volume of the parts. The head inclines somewhat toward the right side, the eyelids are drooping, and the facial expression is immobile. There are no scars on the body, except one in the right popliteal region, the result of an intentional injury in order to avoid military duty. When the patient is raised the upper extremities are flexed at the first interphalangeal joints. The lower extremity is slightly flexed, and there is plantar flexion at the ankle-joints. Fibrillary twitchings are to be seen especially in the right upper extremities, in the muscles of the shoulders, and in the muscles of the mouth, they are present, but to a lesser degree in the muscles of the lower extremity, and here, too, they are more conspicuous on the right side than on the left. The patient is unable to whistle or to blow out the cheeks, and the mouth is characteristically tapir. The tongue is constantly in the state of undulatory movements, and is very much limited in its excursions without and within the mouth. There is considerable spasticity of both upper extremities, and the tendon-jerks are all exaggerated. The atrophy in the upper extremity is most profound in the extensor muscles of the forearms, and the thenar, hypothenar, and interossei muscles. In the lower extremities the thigh muscles on the right side are reduced in volume. Passive movements encounter marked resistance. The knee-jerks are lively, but there is no patellar or ankle clonus. The increase of tendon-jerks in the lower extremities is not proportionate to the profound spasticity. The plantar reflexes are lively. There is no disturbance of sensation or of the sphincters.

Electrical examination gives the following noteworthy information: To faradic and galvanic excitation the muscles at first showed rather increased irritability; this, however, is soon exhausted, and after the current had been applied a few times excitability is lost for a while. The transition is, however, not a sudden one, but it goes slowly from sharp contraction through various stages of vermiform contraction to entire absence of response. The ulnar nerves do not respond to any current.

Some cases of this disease attributed to injury, such as that of Goldberg, are reported so incompletely that neither the existence of amyotrophic lateral sclerosis nor the etiological connection of trauma is clear to the reader. In other cases, such as that reported by Oppenheim, in which the symptoms came on after severe overexertion, there existed symptoms (hyperæsthesia of the left thorax, anæsthesia for temperature, and pain in the right leg) which are never present in typical cases of the disease. On the other hand, there are cases, such as those of Strümpell and others, in which trauma seems to have been the immediate antecedent of the appearance of the disease. Just how trauma acts to disease the motor neurons is not clear. Whether by the depreciation of mental and physical vitality or by the production of metabolic products which act injuriously on the motor neurons to facilitate the occurrence of the disease cannot be said. From a review of all the cases reported it may be said that trauma does not seem to be an adequate cause of the disease. Personally I have never seen a case in which I thought it had the slightest etiological influence. Overwork, and especially overwork of a particular character, such as that of gold-beaters, embroiderers, etc., which calls for exhausting use of certain sets of muscles and which plays a rôle in the etiology of spinal progressive muscular atrophy, does not seem to enter into the etiology of the disease under consideration. It occurs mostly among the working class, but no particular occupation would seem to stand in relation to it.

There is much in the natural history and occurrence of the disease which reminds one of an infectious or intoxication process, and it was with considerable interest that the list of cases that I have selected was looked through to determine if there were any information to be had upon this point.

A number of cases have been reported which developed within a short time after parturition. These may be dependent upon some unknown toxic substance. The following case is an excellent example:

Mrs. P. V., aged thirty-four years, born in Russia, married, and has six children, four of which died in early childhood, two are living and well. She has always had good health. Her present illness began a year ago, immediately after the birth of her last child. She arose the sixth day after a normal labor, and soon experienced an increasing weakness of all of the extremities. Within the next six months this had increased to such an extent that she was unable to get out of a chair or to help herself, as in eating and in dressing, with the upper extremities. There was no complaint of pain or of disturbance of the sphincters. She complains now, December 7, 1895, of a "tension in the nerves" (spannung), and of nervousness, of stiffness of the legs, and of paralysis of the four extremities. Examination at this time shows a woman of medium size, fairly well nourished, lying in bed. She is unable to stand, to sit, to work, or to make any movement except of the head, and limited movements of the upper extremities. The left upper extremity is weaker than the right. There is no difficulty in swallowing, but she says that it requires much effort for her to speak, and her voice is slightly husky. There is pronounced atrophy of the thenar, hypothenar, and interosseous muscles of both hands, more advanced in the right hand. Atrophy of both shoulder girdles, more pronounced on the right than on the left, and distinct fibrillary twitching in the atrophying muscles. The jaw-jerk is very lively, the elbow-jerks are increased, the knee-jerks are somewhat plus, the plantar reflexes are absent. There is no atrophy of the muscles of the lower extremities despite the motor paralysis, but fibrillary twitchings are noted from time to time in the muscles of the thigh. There are no sensory disturbances, the sphincters are intact. The notes of examination, made six months later, are as follows:

The patient has become more helpless. She now has difficulty in swallowing, food frequently gets into the larynx, and liquids often regurgitate, and there is marked disturbance of speech. It is very difficult for her to speak at all when she is lying flat. Respiration is hurried and shallow, and the accessory muscles of respiration are constantly being called into play. The respiratory murmur is scarcely audible. The atrophy of the upper extremity has become more profound. Passive movement of the left shoulder meets with elastic resistance and is painful to the patient. She is still able to elevate the shoulders slightly and to flex and extend the right arm to a very slight extent. She can also make limited movement of the right toes. The atrophy, which involves the supraspinatus, deltoid, muscles of the forearm, the lumbricales, interossei, thenar, and hypothenar eminences, is very advanced on the right side. There is fibrillary twitching in all of the atrophic muscles. The response to galvanic current is sluggish and vermiform, the best contraction being obtained by the kathode. The galvanic reaction is lost in the peroneals, diminished in the nerves of the upper extremities. The faradic irritability is still present but very sluggish. The tendon-jerks are increased; there is considerable spasticity of the upper extremities, less in the lower extremities. The patient now has attacks of spasmodic crying and laughing.

Six of the patients gave a history of syphilis. This is probably not more than the actual percentage of syphilization. In two of these cases, both my own, there may have been some direct relationship between the syphilitic infection and the amyotrophic lateral sclerosis. A brief outline of these cases is as follows:

The patient, a single man, forty-nine years old; was by occupation a house and sign painter. He has never had lead poisoning. When forty-four years old he contracted syphilis, for which he had no treatment save local application. Two years afterward, without apparent or attributable cause, the muscles of the left hand began to atrophy. A few months later the atrophy began in the left leg, and about the same time he began to be slightly spastistic. The atrophy, which was in active progress at the time of his admission to the hospital, now involved both upper extremities, the left more than the right, and to a slight extent the left lower extremity. The tendon-jerks of the knees, ankles, and elbows are much exaggerated, the left more than the right. There is no ankle clonus. The patient complains of stiffness and a feeling of tension in the back of the neck. There are no sensory or sphincteric disturbances. Bulbar symptoms have not yet shown themselves.

In the second case the syphilitic element in the disease seemed to be of much importance. This case is clinically a typical example of amyotrophic lateral sclerosis. Still, it is not unlikely that the pathological process upon which it is dependent is a syphilitic disease of the spinal cord, syphilitic myelitis, if we wish to use that term, the brunt of the lesion being borne by the anterior horns with coincident or secondary involvement of the white matter around them. It is probable that the pathological change in such cases begins in the bloodvessels and constitutes a syphilitic arteritis or endarteritis, and that the changes in the parenchyma are secondary.

A plumber's assistant, aged forty-eight years, contracted syphilis when thirty-six and received treatment until the local manifestations of the disease had disappeared, *i. e.*, for two or three months. He remained well until the end of August, 1902, when, while driving nails into a resistant wall, the left hand wielding the hammer, he experienced a sense of increasing powerlessness in the left upper extremity. He had to quit work, and has not returned to it since. The weakness of the left upper extremity continued to increase, and soon became manifest not only in the shoulder but in the forearm and hand, the flexors being particularly weak. Within a month he remarked some weakness of the muscles of the right forearm and hand, the two middle fingers being weakest. About six weeks after the onset of the symptoms he noticed for the first time atrophy of the muscles of the left shoulder girdle, and later of the muscles of the arm and forearm. Aside from the sensation accompanying fibrillary twitching in the atrophying muscles, the patient made no complaint.

Examination three months after the attributed onset of the disease revealed profound atrophy of the muscles of the left shoulder girdle, the biceps and triceps, and slight atrophy of the pectoral muscles. The flexor muscles of the left forearm are more atrophied than the extensors on the left side, while on the right side this condition is reversed. The tendon jerks are very much exaggerated all over the body. Myotatic irritability is slow. The plantar reflexes are very lively and of the flexor type. The abdominal reflexes are present, and the cremasteric diminished. There is some increased resistance to passive movements of the lower extremities. All forms of sensory stimulation are interpreted correctly. The pupils are reduced to a pin-point and dilate very slightly in the dark.

There are a number of cases similar to this recorded. In some of them the diagnosis of subacute poliomyelitis has been made on account of the rapidity with which the symptoms came on, or because of rather sudden accession to the symptoms. The explanation of such abruptness is, I believe, that one or more diseased bloodvessels ruptured and caused rapid destruction of surrounding nerve cells. I would not be understood to say that I consider these cases genuine examples of amyotrophic lateral sclerosis. The point that I wish to make is, that there are cases of syphilitic disease of the cord (best designated at the present time as focal myelitis) which parallel the symptoms of amyotrophic lateral sclerosis, in the beginning at least, very closely, and that these may be called syphilitic amyotrophic lateral sclerosis.

In the first case the patient's occupation may have had something to do with the development of the disease, for there have been cases recorded in which lead poisoning would seem to have had some relationship to the development of the disease, as in the following case:

A house painter, thirty-five years old, of good habits, and who denied syphilitic infection, gave the following history: Four years before the onset of his present symptoms he had a typical attack of painter's colic, from which he recovered in a fortnight, since when he has kept at his work. A year ago he first noticed weakness of the little finger of the right hand. Soon after the atrophy became evident, not only in the hand, but in the right shoulder girdle. The atrophy was accompanied with marked fibrillary twitchings, "cramped" feeling in the arms, and pain and stiffness of the neck. The knee-jerks, ankle-jerks, and the triceps-jerks are exaggerated, and there is an atypical Babinski reflex. Bulbar symptoms have not yet shown themselves.

In a case of this kind it may be a mere coincidence that the disease occurred in a worker with lead. But knowing, as we do, that lead has a special predilection to attack motor neurons, it may well be that it bore some relationship to the immediate development of the disease in this case. In fact, it may be said that all of the factors that have been attributed as in some manner causative of the disease, such as injuries, exposure, intoxications, and the like, act only as the fuse to ignite the pile that is already prepared. Back of it all is the *something* which is the real cause of the disease.

Finally, a great deal has been written about an innate disposition on the part of the neurons to undergo degeneration when subject to influences which would be innocuous to properly endowed and developed neurons, an abiotrophy of the motor neurons, to use a term recently introduced by Gowers. It must be admitted that the tissues are endowed with a certain vital resistance, and when this wanes off they readily fall a victim to injurious influences, but amyotrophic lateral sclerosis has, in the main, the clinical features of an active destructive disease, not a decay. Although I am willing to admit prenatal influences, there must be some more tangible and actively operative cause. It is not unlikely that we must look to the pathological chemist for the discovery of the real noxious agency.

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CONGENITAL DISLOCATION OF THE SHOULDER.

By Charles Greene Cumston, M.D.,
of Boston.

Congenital dislocation of the shoulder is of infrequent occurrence, and recorded cases of this affection are still very few in number and some of them are of doubtful value. Instances are recorded in adults and it is only on more or less certain commemoratives that the congenital nature of the condition has been diagnosed. Other cases have been met with in the fœtus, but in these a detailed account is wanting.

I have endeavored to collect all reported cases of congenital dislocation of the shoulder, but there are only a few that are really conclusive.

Many of them appear to me simply traumatic dislocations occurring during delivery, and in these cases the condition is usually a separation of the epiphysis, while others are instances of infantile paralysis. Still others are simply a diastasis due to a relaxation of the ligaments; while still others appear to have a distinctly congenital origin, which is proven by an electrical examination of the muscles or by post-mortem examination. In this paper I shall deal only with the two latter conditions.

The history of congenital dislocations goes back to Hippocrates, who speaks of them in several passages of his writings, but since his time the attention of surgeons was nearly turned away from this congenital defect until that great master, Ambroise Paré, again called attention to this type of lesion, although he appears to have had the traumatic obstetrical type more in view, for he says: "Car souventes fois les luxations arrivent aux enfantements difficiles quand les sages-femmes, tirant les bras des enfants, disloquent les iouointures de